REMARKS

Upon entry of the present amendment, claims 1, 2 and 4-7 are pending in this application. Claim 3 is cancelled as drawn to a non-elected invention. Applicants reserve the right to pursue the subject matter of this claim in one or more continuing applications. No new matter is added.

Rejections under U.S.C.§ 102

Claims 1, 2 and 4-7 are rejected under 35 U.S.C. § 102(e), as being anticipated by Wagle et al., U.S. Patent Application Publication 2002/0022622 ("Wagle"). According to the Examiner, although Wagle does not specifically teach decreasing intraocular pressure or improving ocular accommodation in an animal in need thereof, Wagle does disclose the target patient population embraced by the instant claims. The Examiner further states that Wagle discloses a method of treating diabetic retinopathy in a patient by administering 2,4,5-trimethylthiazole and therefore a decrease in intraocular pressure or an improvement in ocular accommodation in the patient would be an inherent characteristic of the disclosed method. *See*, Office Action at page 3.

Claim 1, from which the remaining clams subject to the rejection properly depend, recites "... method of decreasing intraocular pressure or improving ocular accommodation in an animal in need thereof..." Applicants agrees with the Examiner that Wagle does not explicitly disclose decreasing intraocular pressure or improving ocular accommodation in an animal in need thereof. However, Applicants disagree with the Examiner's assertion that Wagle inherently discloses decreasing intraocular pressure or improving ocular accommodation in an animal in need thereof.

It is well established that "in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of

circumstances is not sufficient.' " In re Robertson, 169 F.3d 743, 49 USPQ2d 1949 (Fed. Cir. 1999). In order to find inherent anticipation, the undisclosed element of the prior art had to be a necessary technological fact of the prior art. Continental Can Co. v. Monsanto Co. 948 F.2d 1264, 20 U.S.P.Q.2d (BNA) 1746 (Fed. Cir. 1991). It is inadequate to show that the prior art process would probably, or possibly, produce the undisclosed element. Id. Rather, the undisclosed element had to flow as a natural consequence from the technological constraints of the prior art. Id.

Therefore, the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. In re Rijckaert, 9 F.3d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993) (emphasis in original).

The present specification discloses methods of treating or ameliorating glaucoma, decreasing intraocular pressure and increasing ocular accommodation by administering the thiazole, imidazole and oxazole compounds of Formula I or Ia to subjects in need thereof. Wagle discloses methods of treating or ameliorating diabetes or diabetic retinopathy by administering the thiazole, imidazole and oxazole compounds of Formula I or Ia to subjects in need thereof. As stated by the Examiner, Wagle does not disclose glaucoma, intraocular pressure or ocular accommodation. Thus to establish that Wagle inherently anticipates the present claims, the Examiner must establish that the undisclosed element of the prior art (*i.e.*, glaucoma, intraocular pressure or ocular accommodation) must necessarily flow as a natural consequence from the disclosure of Wagle. Applicants respectfully submit that the Examiner has failed to meet this threshold.

One of ordinary skill in the art would readily recognize that the etiology, symptoms and treatment of glaucoma/increased intraocular pressure is quite different from that of diabetic retinopathy.

The eye constantly produces aqueous humor, the clear fluid that fills the anterior chamber (the space between the cornea and iris). The aqueous humor filters out of the anterior chamber through a complex drainage system. The delicate balance between the production and drainage of aqueous humor determines the intraocular pressure. Normal human intraocular pressure ranges between 8mm and 21mm Hg. Increased intraocular pressure indicates a problem with the amount of aqueous humor in the eye: either the eye is producing too much, or it's not draining

properly. High intraocular pressure is a major risk factor for glaucoma. Glaucoma is an eye disorder that causes progressive and irreversible optic nerve damage and vision loss.

Although not everyone with intraocular pressure above 20mm Hg develops glaucoma, someone with the pressure over 20mm Hg is more likely to develop glaucoma than someone with a lower pressure. Also, there are some people who have an intraocular pressure below 20mm Hg who develop glaucoma, this is called normal tension glaucoma.

Depending on the type of glaucoma, various symptoms may be experienced. There is gradual loss of peripheral vision and night vision. Blurred vision and colored rings around lights accompany these symptoms. If intraocular pressure remains high, tunnel vision can develop.

Glaucoma Risk factors include age, race (African-Americans and persons of Japanese decent have a higher incidence of glaucoma), sex (females are high risk), family history and medical disorders (*e.g.*, presence of hyperopia or farsightedness, diabetes or previous eye injury). Although glaucoma cannot be cured, in most cases it can be successfully controlled. Glaucoma treatment entails decreasing aqueous humor production, increasing fluid drainage or a combination of the two, thereby decreasing intraocular pressure. Intraocular pressure treatment may be in the form of medication (*e.g.*, eye drops containing beta-blockers or alpha-2 agonists), laser therapy or surgery (*e.g.*, trabeculoplasty, trabeculectomy). *See*, Haimes Declaration ¶ 6.

Diabetic retinopathy is a disorder of the retinal blood vessels resulting from diabetes. Everyone who has diabetes is at risk for developing diabetic retinopathy, but not all diabetics do develop it. The incidence of diabetic retinopathy increases with the duration of diabetes. About 60% of patients having diabetes for 15 years or more will have some blood vessel damage in their eyes and a percentage of these are at risk of developing blindness. Patients with diabetic retinopathy are also at a greater risk of developing retinal tears and detachment.

In diabetic retinopathy, the small blood vessels that are in the retina are damaged and become leaky. New blood vessels can also grow in the back of the eye. These new vessels are abnormal and bleed easily, sometimes filing the back of the eye with blood. This causes the retina to swell and form deposits. The affect of diabetic retinopathy on vision varies widely, depending on the stage of the disease. Some common symptoms include blurred vision, floaters and flashes and sudden vision loss. Risk factors for diabetic retinopathy include high blood glucose, poor diet and lack of exercise.

Diabetic retinopathy is treated in many ways, depending on the stage of the disease and the specific problem that requires attention. The preferred method of treatment is laser photocoagulation to seal off leaking blood vessels and destroy new growth or in more extensive cases, vitrectomy. Many patients control their diabetes with diet and medication to delay or prevent the development of diabetic retinopathy and other complications.

Although diabetes and diabetic retinopathy are risk factors for increased intraocular pressure and glaucoma, not all diabetics or people suffering from diabetic retinopathy develop increased intraocular pressure or glaucoma. In fact, while most diabetics develop diabetic retinopathy over time, the same cannot be said for intraocular pressure and/or glaucoma. Specifically, the instant specification teaches that primary open angle glaucoma (the predominant form of glaucoma) occurs in approximately 4% of diabetics compared to 1.8% of the general population. *See*, page 1, lines 18-32. *See*, Haimes Declaration ¶ 7.

Applicants submit that to establish inherency, it is inadequate to show that a diabetic or subject suffering from diabetic retinopathy would probably, or possibly, develop glaucoma or intraocular pressure despite the fact that diabetes is a risk factor for developing glaucoma or increased intraocular pressure. One of ordinary skill in the art would readily recognize that while diabetics are twice as likely to develop glaucoma as compared to the general population, glaucoma is not a natural consequence that necessarily flows from diabetes or diabetic retinopathy (Emphasis Added). *See*, Haimes Declaration ¶ 8.

For the foregoing reasons, Wagle does not teach or suggest, explicitly or inherently, all of the limitations of the claimed invention. Accordingly, Applicants assert that claims 1, 2 and 4-7 are not anticipated by Wagle and respectfully request this rejection be withdrawn.

CONCLUSION

On the basis of the foregoing amendment and remarks, Applicants respectfully submit that the pending claims are in condition for allowance and a Notice of Allowance for the pending claims is respectfully requested. If there are any questions regarding this application that can be handled in a phone conference with Applicants' Attorneys, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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